IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Reissue Application of:	Pines et al.
for Reissue of:	U.S. Pat. No. 6,028,075
Issued:	February 22, 2000
Based on Ser. No.:	08/797,703
Filed:	February 11, 1997
Entitled:	QUINAZOLINONE CONTAINING PHARMACEUTICAL COMPOSITIONS FOR PREVENTION OF NEOVASCULARIZATION AND FOR TREATING MALIGNANCIES

Atty. Docket No.: CGD-002.0 US

Asst. Commissioner for Patents
BOX REISSUE
Washington, D.C. 20231

REISSUE APPLICATION PURSUANT TO 35 U.S.C. §251

Sir:

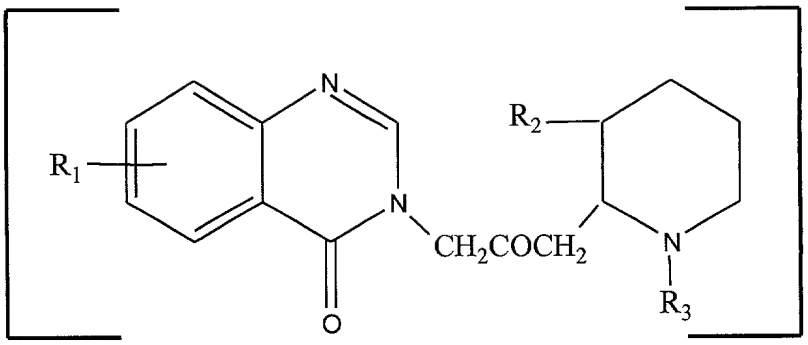
Pursuant to 35 U.S.C. §251, Reissue Applicants hereby request reissue of the above-referenced U.S. Pat. No. 6,028,075, to correct an error in the chemical formulary appearing throughout the specification and claims for a certain group of quinazolinone compounds including halofuginone, said error resulting in the patent being partially inoperative.

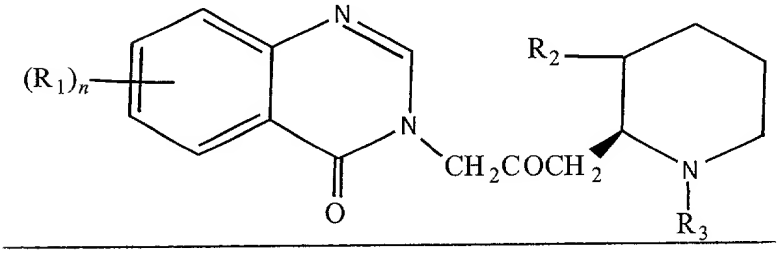
Please amend the specification and claims according to 37 C.F.R. §1.173, as follows:

IN THE SPECIFICATION:

At column 3, beginning at line 62, please amend the paragraph as follows:

Such a type-specific collagen synthesis inhibitor is disclosed in U.S. patent application Ser. No. 08/181,066 for the treatment of a fibrotic condition, restenosis or glomerulosclerosis. This specific inhibitor is a composition with a pharmaceutically effective amount of a pharmaceutically active compound of a formula:





wherein:

n is 1 or 2

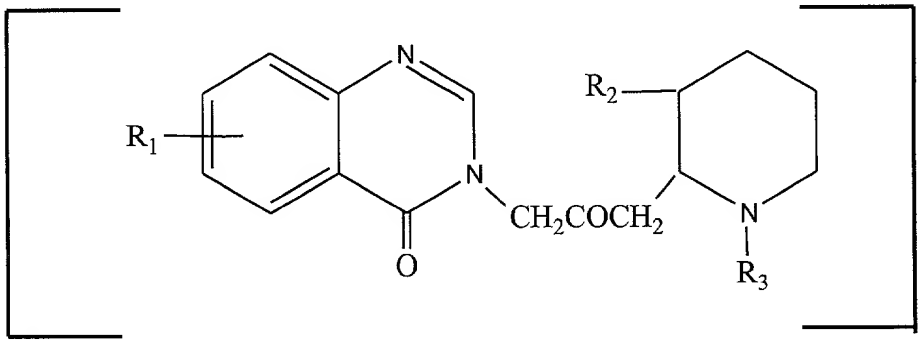
R_1 is a member of the group consisting of hydrogen, halogen, nitro, benzo, lower alkyl, phenyl and lower alkoxy;

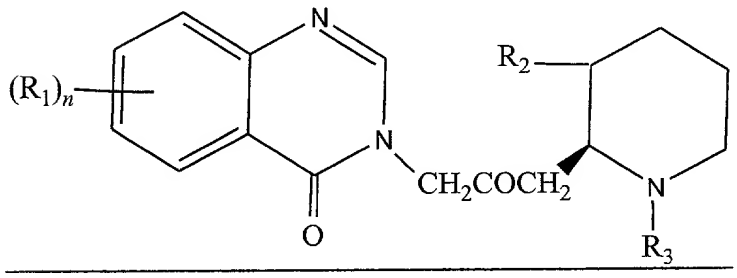
R_2 is a member of the group consisting of hydroxy, acetoxy and lower alkoxy, and

R_3 is a member of the group consisting of hydrogen and lower alkenoxy-carbonyl. Of this group of compounds, Halofuginone has been found to be particularly effective for such treatment.

At column 5, beginning at line 10, please amend the specification as follows:

According to an embodiment of the present invention, there is provided a composition and a method for treating a tumor, including a pharmaceutically effective amount of a compound in combination with a pharmaceutically acceptable carrier, the compound being a member of a group having a formula:





wherein:

n is 1 or 2;

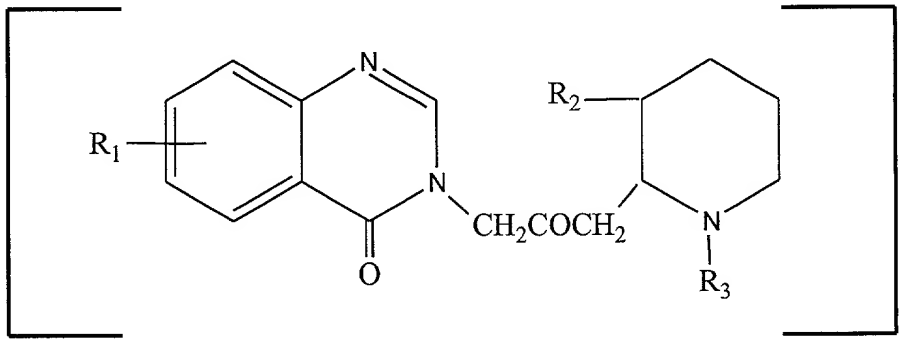
R_1 is a member of the group consisting of hydrogen, halogen, nitro, benzo, lower alkyl, phenyl, and lower alkoxy;

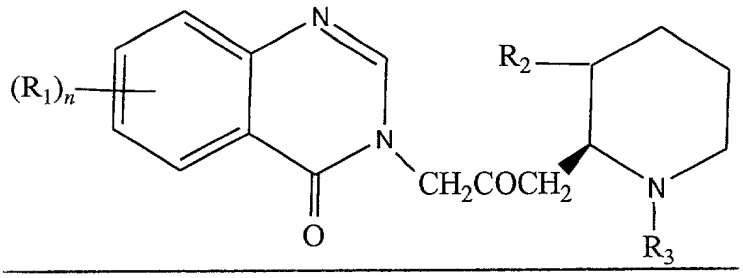
R_2 is a member of the group consisting of hydroxy, acetoxy, and lower alkoxy, and

R_3 is a member of the group consisting of hydrogen and lower alkenoxy-carbonyl.

At column 5, beginning at line 35, please amend the specification as follows:

According to another embodiment of the present invention, there is provided a method of manufacturing a medicament for treating a tumor, including the step of placing a pharmaceutically effective amount of a compound in a pharmaceutically acceptable carrier, the compound being a member of a group having a formula:





wherein:

n is 1 or 2;

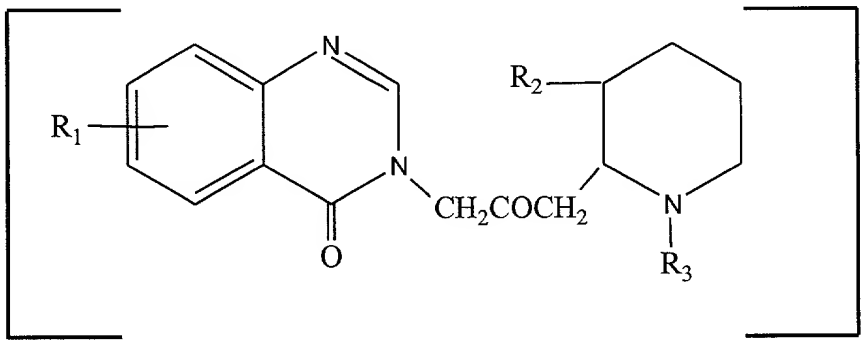
R_1 is a member of the group consisting of hydrogen, halogen, nitro, benzo, lower alkyl, phenyl, and lower alkoxy;

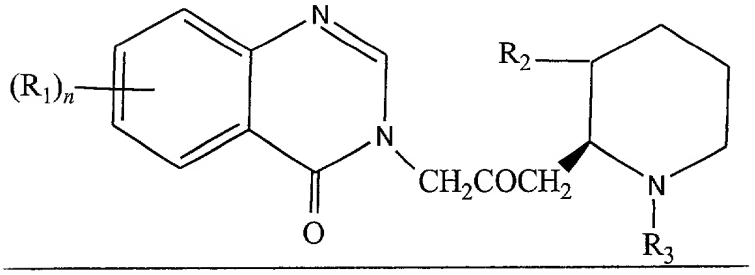
R_2 is a member of the group consisting of hydroxy, acetoxy, and lower alkoxy, and

R_3 is a member of the group consisting of hydrogen and lower alkenoxy-carbonyl.

At column 5, line 61 to column 7, line 18, please amend the specification as follows:

According to yet another embodiment of the present invention, there is provided a method of manufacturing a medicament for substantially inhibiting neovascularization, including the step of placing a pharmaceutically effective amount of a compound in a pharmaceutically acceptable carrier, the compound being a member of a group having a formula:





wherein:

n is 1 or 2;

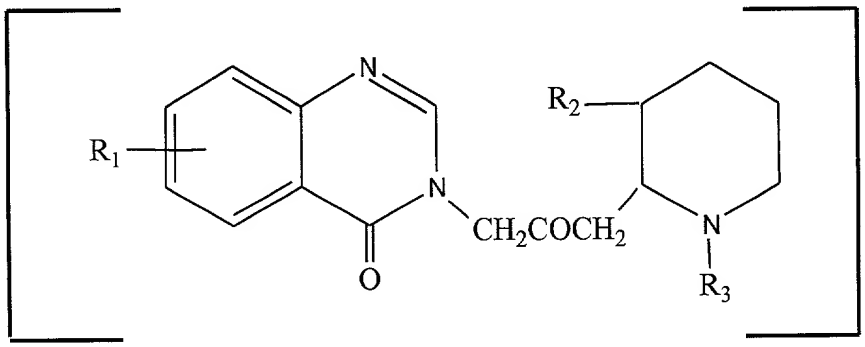
R_1 is a member of the group consisting of hydrogen, halogen, nitro, benzo, lower alkyl, phenyl, and lower alkoxy;

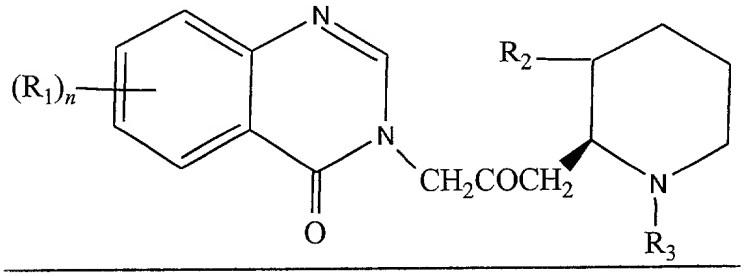
R_2 is a member of the group consisting of hydroxy, acetoxy, and lower alkoxy, and

R_3 is a member of the group consisting of hydrogen and lower alkenoxy-carbonyl.

At column 6, beginning on line 19, please amend the specification as follows:

According to still another embodiment of the present invention, there is provided a method for the treatment of angiogenesis in a subject, including the step of administering a pharmaceutically effective amount of a compound having a formula:





wherein:

n is 1 or 2;

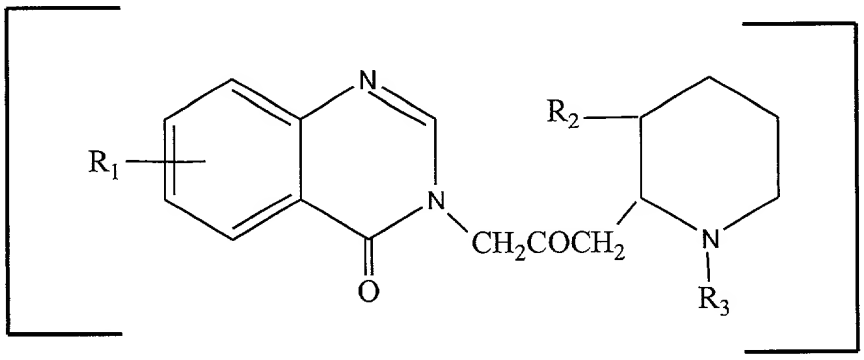
R_1 is a member of the group consisting of hydrogen, halogen, nitro, benzo, lower alkyl, phenyl, and lower alkoxy;

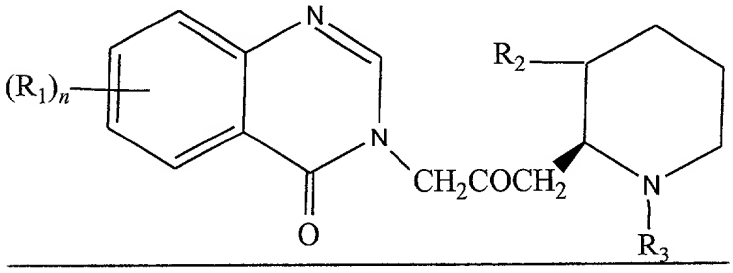
R_2 is a member of the group consisting of hydroxy, acetoxy, and lower alkoxy, and

R_3 is a member of the group consisting of hydrogen and lower alkenoxy-carbonyl.

At column 6, beginning on line 42, please amend the specification as follows:

According to still another embodiment of the present invention there is provided a method for the treatment of a tumor in a subject, including the step of administering a pharmaceutically effective amount of a compound having a formula:





wherein:

n is 1 or 2;

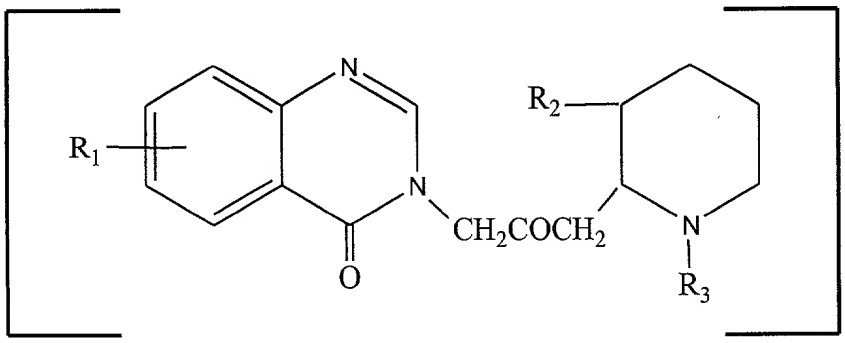
R_1 is a member of the group consisting of hydrogen, halogen, nitro, benzo, lower alkyl, phenyl, and lower alkoxy;

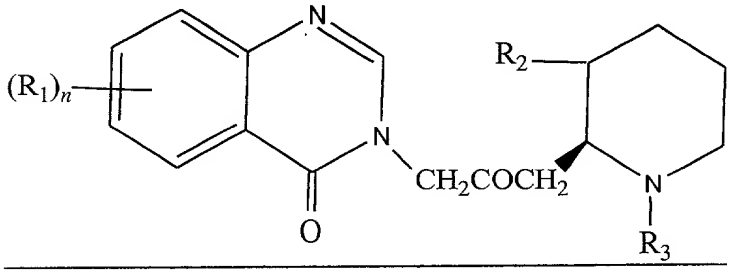
R_2 is a member of the group consisting of hydroxy, acetoxy, and lower alkoxy, and

R_3 is a member of the group consisting of hydrogen and lower alkenoxy-carbonyl.

At column 6, line 64, to column 7, line 17, please amend the specification as follows:

There is also provided a composition for inhibiting cell proliferation enabled by a deposition of an extracellular matrix, including a pharmaceutically effective amount of a compound having a formula:





wherein:

n is 1 or 2;

R_1 is a member of the group consisting of hydrogen, halogen, nitro, benzo, lower alkyl, phenyl, and lower alkoxy;

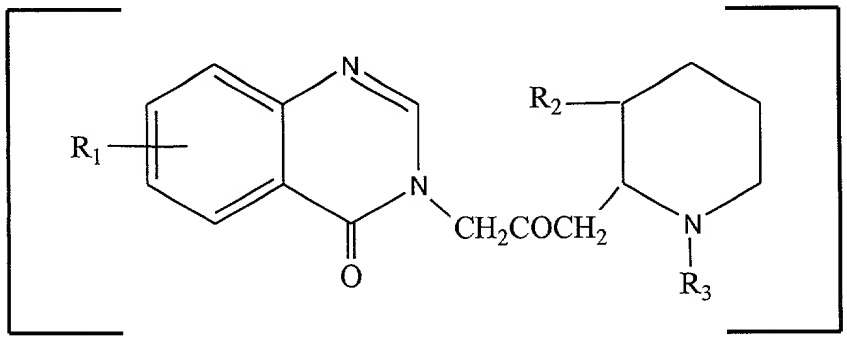
R_2 is a member of the group consisting of hydroxy, acetoxy, and lower alkoxy, and

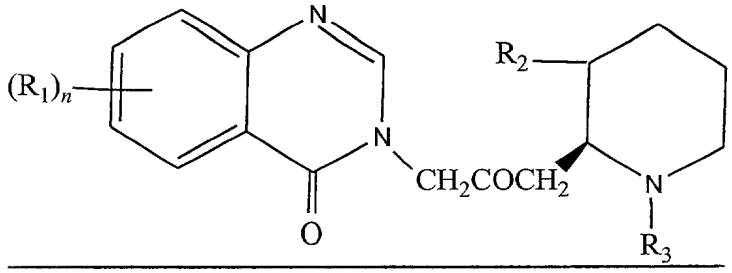
R_3 is a member of the group consisting of hydrogen and lower alkenoxy-carbonyl.

IN THE CLAIMS:

Please amend Claim 1 as follows:

1. (Amended) A method for the treatment of a tumor sensitive to the compounds below in a subject, comprising the step of administering a pharmaceutically effective amount of a compound having a formula:





wherein:

n is 1 or 2;

R_1 is a member of the group consisting of hydrogen, halogen, nitro, benzo, lower alkyl, phenyl, and lower alkoxy;

R_2 is a member of the group consisting of hydroxy, acetoxy, and lower alkoxy, and

R_3 is a member of the group consisting of hydrogen and lower alkenoxy-carbonyl.

REMARKS

Reissue Applicants request that the preceding amendments to the specification and claims be made to correct the general formula for the group of substituted quinazolinone compounds described in the specification and claims of U.S. Pat. No. 6,028,075. Pursuant to 35 U.S.C. §251, Applicants request correction and reissuance of this partially defective patent.

Specifically, the formula for the group of quinazolinone compounds which includes the preferred compound, halofuginone, is corrected in the above amendments to define the number of "R_1" substituents that may be present on the quinazolinone fused ring structure, that number being represented by subscript variable "n", which is defined as being "1 or 2" below the formula. Also, the inadvertent ommission of the term "-carbonyl" at column 5, line 34 is corrected.

The necessary correction of the formula is obvious, taking the specification and claims as a whole into account. The only change to the formula is to specify that there may be more than one R_1 substituent, and that where there are two such substituents, they may be different. The presence of at least one R_1 substituent group is supported by the formula as it appears in the original patent; the instance where there are two R_1 substituent groups and that they must be independently selected (i.e., may be different) is supported by the specific reference throughout the specification to the preferred compound, halofuginone (7-bromo-6-chloro-3-[3-(3-hydroxy-2-piperidyl)-2-oxopropyl]-4(3H)-quinazolinone), in which there are two R_1 substituents (bromo and chloro) attached to the quinazolinone structure. See, for example, dependent Claim 2, specifically reciting halofuginone. Correction of the formula is necessary to harmonize Claim 2 reciting the preferred compound with the general formula of the independent claim.

Further support for the corrected formula substituted by the foregoing amendments may be found in Pines et al., U.S. Pat. No. 5,449,678, which is referred to in the present patent at

column 4, line 20, at column 4, line 35, column 4, line 45, and at column 6, line 26. It is evident from Applicants' disclosure that the complete formula from the cited patent was intended to be transcribed in the specification of the present patent.

No new matter has been added by these amendments.

Clarification of the structural formulas as described above and reissuance of the patent are respectfully solicited.

Respectfully submitted,

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